Examples of Well Written and Poorly Written Critiques

A. EXAMPLES OF WELL WRITTEN BULLETED CRITIQUES:

OVERALL IMPACT

Example 1, Score = 2

Strengths

- These investigations should identify new molecular therapeutic targets to improve current therapies for the care of Q cancer patients at early and late stages of disease progression.
- The project is based on a solid rationale and hypothesis, and is supported by strong preliminary data and recent publications from this laboratory.
- The role of X and Y pathways in malignant transformation of Q cells adds a high degree of innovation.
- The overall impact on understanding basic mechanisms of Q carcinogenesis with implications for development of novel molecular therapeutics is likely to be very high.

Weaknesses

- There are negligible weaknesses related to the definition of cancer stage.

Example 2, Score = 7

Strengths

- These experiments may provide some information about association of certain modified genes with development of XYZ.

Weaknesses

- It is a major weakness that the entire project is superficial. The plan to study the modified genes is unclear and there is no explanation for how this information would be further developed for a better understanding of XYZ.
- There is no indication, rationale or justification for how the thousands of modified genes that may be identified will be selected and prioritized for further study in this aim.
- The success of aim 1 is based on the unknown functional significance of genes identified in aim 2.
- The productivity of the PI is moderate, with only three publications in moderate impact journals in the past two years.
- The correlation between modification of various genes and XYZ is already known.
- Overall, the project is likely to have only an incremental impact on the field of XYZ because there is no real plan for logical analysis of any new modified genes identified in this study.

Example 3, Score = 3 (This example is related to behavioral and health services research. Two other examples for critiques in this field are given at the end of this document)**

Strengths

- There is little currently known about the direct and indirect costs associated with XYZ clinical condition and treatment and the existing evidence may be biased due to the retrospective nature of the data collection and the presence of recall bias, and/or inaccurate due to small sample sizes for prospective studies.
- By conducting both a retrospective and a prospective survey, investigators will be able to examine whether existing (retrospective) studies have biased estimates of the costs of XYZ. The preliminary study indicates that retrospective studies are likely to underestimate costs in certain areas.
- The cost categories are comprehensive and include both direct and indirect costs and short and long run costs for multiple sectors.

- The results of this project could be quickly incorporated into effective policies.

Weaknesses

- A research assistant may not be experienced enough to be responsible for the day-to-day operation of the project, including make-or-break aspects such as conducting patient interviews.
- The application does not describe how some costs of XYZ condition and treatment will be calculated.

SIGNIFICANCE

Example 1, Score = 6

Strengths

- The control of Q cell differentiation is an important aspect of XY immunity.
- Z1 may have important roles in Q cell development, including the regulation of terminal differentiation.
- Together with Z1, Z2 may regulate X, Y and W transcription.

Weaknesses

- Outcomes presented and the discussion of its significance in the application indicates a lack of understanding of Q cell development. The figure purporting to show flow cytometry of pro-Q and pre-Q cells in normal spleen does not do so.
- The phenotype of the Z1 knockout mice is unclear. Figures and data are inadequately described with a lack of details. It is not clear which stages of Q cell development are affected in these mice.
- W1 expression is reduced in spleens of Z1 knockout mice, but plasma cell numbers and markers were not addressed in detail.
- Y1-mediated deletion of Z2 genes may not effectively address roles of Z2 in late Q cell differentiation. The investigator needs to demonstrate that the mice will be useful for studies of QRS cell differentiation.

Example 2, Score = 3

Strengths

- Non-pharmacologic treatment for XYZ is needed. Women with XYZ need a means to combat obesity, insulin resistance, and infertility without relying on drugs that have side effects or compromise fertility. Use of WXY may reduce insulin resistance when used alone or ultimately in combination with other treatments such as diet or weight loss.
- This study will demonstrate efficacy of WXY in promoting ovulation, and will delve into the molecular mechanism through which WXY acts, potentially through QR. A comprehensive battery of measures includes ABC and DEF.

Weaknesses

- It would be surprising if a simple dietary supplement in isolation were to have an effect as profound as that which is hypothesized.

INVESTIGATOR(S)

Example 1, Score = 1

Strengths

- The Principal Investigator has outstanding qualifications to direct the proposed research. He/she is a pioneer in the field of XYZ and has made significant contributions to the development of methodology in the field.
- The collaborators in the team bring in additional expertise in imaging techniques. The collective level of expertise of this group is a great strength.

- There is long history of strong collaboration among the team members.

Weaknesses

- There is no notable weakness.

Example 2, Score = 5

Strengths

- The Principal Investigator has suitable experience in this research area, and he/she is an expert in the treatment of solid tumors with Z.
- The co-investigator is an expert in the measurement of X. His expertise is an excellent complement to that of the PIs.

Weaknesses

- A biostatistical consultant will participate only at the end of the study for analysis of the acquired data. There is a concern that this service may be needed at earlier stages of the study as well.
- The need for the other collaborators listed as subcontracts is unclear. There is no information or justification provided as to what these collaborators will be doing.
- There is a minor concern that the PI and his collaborator have not been working together before.

INNOVATION

Example 1, Score = 1

Strengths

- Most methodology is relatively standard for the chosen experimental systems, but the concepts (as explained below) are highly novel.
- Concept of X control of a stress response is highly innovative.
- Concept of multiple layers of YZ regulation by signaling and modification in a tissue-specific manner is a novel hypothesis that will move the field forward.
- Justification and choice of model system to study this idea in an experimentally tractable multicellular organism is relatively unique and innovative.

Weaknesses

- None noted by reviewer.

Example 2, Score = 7

Strengths

- In general, less is known about XYZ clinical practice environment than about other clinical environments

Weaknesses

- A large body of research already exists on organizational readiness for change.
- Psychometrically sound measures of organizational change exist. Adaptation to the proposed clinical environment represents only minor innovation.
- Methods and data analytic approach are not innovative.

APPROACH

Example 1, Score = 3

Strengths

- Proposed studies are based on compelling preliminary data demonstrating that every assay that will be used is working and in hand.

- Studies are hypothesis-driven, well-described and have a high likelihood to generating new information on how Y modulates Z mediated activity.
- The development of the XYZ assay will allow for very precise analysis of the most poorly understood step in the ABC activation pathway. As such the development of this assay should have been very useful for this study as well as a major advance for the field.
- The Principal Investigator will use both cell-based as well as virus-based assays to evaluate the activation mechanism, which is viewed as important and is a strength.
- The investigator has in hand a collection of mutants with varying phenotypes that will be useful in these studies.

Weaknesses

- Some of the data interpretation is discussed in generalities and mainly focuses on how studies would confirm what has already been published.
- While XY will be useful for evaluating large changes in various mutants, the value of its use as described in the application is over inflated.

Example 2, Score = 7

Strengths

- A variety of methods will be used to explore the use of omics technologies, offering a broad strategy to attack the research problem.

Weaknesses

- The actual objectives and experimental plan are poorly defined.
- Examples of possible outcomes are not given.
- There is no contingency plan; therefore it is unclear what can be learned if things do not turn out as planned.
- There is a lack of quantitative milestones in the application upon which to judge its success. It is unclear how sensitive the assay needs to be, what the detection limit should be, how accurate the assay needs to be, and/or how fast it must be performed.
- This application doesn't provide any sort of road map to show the progression of work.
- It is unclear how the measurements the PI proposes would further our understanding of the proposed problems.
- The proposed data analysis does not seem adequate for the type of expected results. The time dependence of the proposed measurements cannot be adequately evaluated with a simple ANOVA test.

ENVIRONMENT

Example 1, Score = 1

Strengths

- The clinical and research facilities are strengths of this application.
- The Investigator has established effective collaborations with experienced investigators both within and outside of the home institution which will provide the needed technologies.
- The sites of collaboration provide facilities that are unique and are necessary for the completion of these studies.

Weaknesses

- None.

Example 2, Score = 6

Strengths

- The Principal Investigator and investigative team have successfully collected data from this site in the past.

Weaknesses

- Samples will have to be shipped for subsequent analysis and, given the circumstances, there is a higher than normal risk of losing samples.
- There is no documentation from the appropriate authorities giving permission to conduct the study at the chosen site.
- There do not appear to be specialized animal facilities or experienced investigators and/or staff identified for handling the proposed transgenic animal experiments.

B. EXAMPLES OF POORLY WRITTEN BULLETED CRITIQUES

OVERALL IMPACT

Example 1, Score = 4

Strengths

- This is a study to investigate the effects of X on Y through activation of the Z cascade. Aims are directed towards identifying responding cell types and the differentiated products, dissection of the Z cascade components that contribute, a search for mechanisms, and effects of systemic administration of Q on inflammatory Y production. Main strengths are the experience of the investigator and published results.

Weaknesses

- Because of a focus on the use of recombinant X, the physiological relevance of their previous and proposed studies is in question. This is a major concern for the project.
- Additional concerns include the preliminary nature of Aims 3-4 (and to some extent aim 2, which is based on effects of a relatively nonspecific Y inhibitor).

PROBLEM: The Strength is mostly a description of the application. The only real strength mentioned is contradicted by the first weakness.

Example 2 - Not Discussed

Strengths

- New investigator;
- Important area of study;
- Interesting preliminary data.

Weaknesses

- PI does not have a strong publication record in the proposed study;
- Additional functional data would be helpful;
- Lack of feasibility in some experiments;
- Somewhat ambitious.

PROBLEM: This is for a ND application. Comments are too vague and brief. "Somewhat ambitious" is not a helpful term.

SIGNIFICANCE

Example 3 - Score = 4

Strengths

- XY represents an important clinical entity with accompanying high morbidity – treatments that improve patient quality of life are needed.

Weaknesses

- None.

PROBLEM: This single bullet does not address what it is about this particular study that is significant – only the significance of the disease is cited. The absence of weaknesses does not match the score.

INVESTIGATOR(S)

Example 1, Score = 3

Strengths

- The PI received his/her PhD in Xology from the University of ABC in 1995, did postdoctoral training at the DEF Clinic, and since 2000 has been at the University of XYZ where he/she is currently the Interim Director of the Clinical Studies Laboratory.

Weaknesses

- Most of the PI's bibliography is on clinical aspects of MNO agents in the Xology setting, with no publication history in the diseases and therapeutic approaches outlined in this application.

PROBLEM: The Strength is a discussion of the PI's training and background, which is not useful here. There is no actual statement of strength to justify the score.

Example 2, Score = 5

Strengths

- The investigator is a leader in the field with a solid track record of publications. There is a significant amount of preliminary results provided in the application demonstrating that the proposed experiments are feasible.

Weaknesses

- Figure annotation and figure legends are absent, inadequate and/or difficult to understand. For example, Figure 1 has no label for the x-axis. Is XYZ labeling two separate bars or are the bars grouped. Similarly, what is meant by "naïve"? Is this referring to untreated? If these are all patients with ZZ antibodies, is there a negative control? Figures should have linear bands quantitated relative to the total protein levels. Include complete figure legends.
- Streamline the preliminary data. A lot of data is shown but it is not clear to the reader where you are going. To clarify the writing, it would help to have a model so the preliminary data can be synthesized and fit into a larger picture.

PROBLEM: This is not consistent with the score, and the discussion of preliminary results does not apply here. The Weaknesses appear to be geared toward a manuscript review, rather than a grant review, and don't belong in the investigator section. The style and content are totally inappropriate.

INNOVATION

Example 1, Score = 5

Strengths

- This is not an innovative application.

Weaknesses

- None.

PROBLEM: The comment on Strength is a weakness, and belies the statement that there were no weaknesses, which also contradicts the score. This is not useful.

APPROACH

Example 1, Score = 3

Strengths

- Several genetically engineered transgenic mouse lines containing constitutively active X as well as knocked out Y and Z genes have been generated. Additionally, various vectors encoding various forms of X and other relevant molecules are also available. The PI's laboratory has experience working with these reagents and systems, and for the most part feasibility for the proposed experiments has been established.
- Aim 1 will use Q cells containing constitutively active, knocked out X, or knocked out Y in microscopy-based experiments to examine how X and Y regulate the dynamics of Q cell/Z interaction. These experiments have a somewhat descriptive feel, although given the connection between these molecules and XX function and YY signaling that was established in the previous funding period, these studies appear to be a logical next step that is likely to yield interesting informative results.
- Aim 2 will analyze the role of X and Y in Z signaling and compartmentalized V signaling as well as the impact of these molecules on Q cell function. These studies are logical and interesting, and will be conducted using confocal methodologies and cellular readouts that are established in the PI's lab.
- Aim 3 will follow up the preliminary observation that X facilitates Q differentiation by examining the role of X induced A, B, C, and D activities. These experiments are all feasible and logical extensions of the preliminary studies, and likely to yield interesting results.

Weaknesses

- XYZ is a central technique in Aim 1. The PI does not have previous experience using this technology, although he/she will be collaborating with Dr. B who runs an imaging core that supports this technology. Dr. B does not, however, appear to have experience using this technology to analyze *in situ* behavior of Q cells, and thus some preliminary data demonstrating that the investigators are comfortable using this technology would increase confidence that this aim can be successfully completed.

PROBLEM: These are not really bullets, but whole paragraphs, with lots of description of the application.

ENVIRONMENT

Example 1, Score = 5

Strengths

- The environment is outstanding.

Weaknesses

- None significant.

PROBLEM: This gives no information and is not consistent with the score.

C. DERIVING OVERALL IMPACT SCORES

This is NOT an average of the criterion scores. See document on definition of overall impact, and how to distinguish this from significance.
(http://grants.nih.gov/grants/peer/guidelines_general/impact_significance.pdf**)**

Example 1

Significance	**2**	
Investigator	**1**	
Innovation		**2**
Approach		**8**
Environment	**1**	

Overall Impact = 6

The average of the criterion scores is about 3. But the very weak approach means that the proposed research plan is not likely to be successful, and so the overall impact score is much worse.

Example 2

Significance	**1**	
Investigator	**1**	
Innovation		**2**
Approach		**1**
Environment	**1**	

Overall Impact = 2

This is an outstanding application, which suffers from a minor weakness in the area of innovation. While the average should give a score close to 1, the presence of even a minor weakness, makes the score 2.

Example 3

Significance	**1**	
Investigator	**3**	
Innovation		**1**
Approach		**3**
Environment	**5**	

Overall Impact = 2

Here the average of the criterions scores would be 3. But the reviewer has decided that despite some weaknesses in the environment, and some other minor weakness, the significance and innovative nature of the application for this field of research is so high, that the overall impact makes it an outstanding application.

D. ** Below are two further examples of well written Critiques in the field of Biobehavioral and Health Services Research for Overall Impact:

Example 4, Score = 2

Strengths

- The proposed study addresses critical gaps in the identification of XYZ, which can become chronic and burdensome left untreated
- The case for utilizing this clinical tool to improve Primary Care Providers' screening and management of XYZ is strong.
- Because there is a strong existing link to clinical settings, the likelihood of obtaining. clinically important results is high- patients are available for recruitment and the research is driven by a well-documented, existing clinical problem.

Weaknesses

- Minor design issues and an ambitious plan are minor weaknesses.

Example 5, Score = 2

Strengths

- The study addresses the critical topic of unmet treatment need among XYZ population, with the potential to identify sources of disparity in treatment utilization and to reduce the impact of treatment disparities on clinical outcomes over time.
- The proposed study seizes a rare opportunity to link two comprehensive clinical databases to address important clinical research questions.
- Key methodological issues and potential challenges in linking and analyzing data have been addressed.

Weaknesses

- No significant weaknesses are noted other than the limitations inherent in relying on existing databases.

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